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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,043	12/21/2001	Wilson Burgess	CI-0013	7597

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 02/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,043	BURGESS ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-48,50-52 and 54-104* is/are pending in the application.

4a) Of the above claim(s) *1,4,5,15-26,29-38,42-48,54-80 and 89-104* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *2,3,6-14,27,28,39-41,50-52 and 81-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/29/2003; 4/05/2002; 2/27/2003.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 2, 3, 6-14, 27, 28, 39-41, 50-52 and 81-88 are under examination.

Claims 1, 4, 5, 15-26, 29-38, 42-48, 54-80 and 89-104 are withdrawn from consideration as drawn to nonelected groups of inventions (I and III-VII) and nonelected "species". Claims 49 and 53 are canceled by applicants [12/09/2003].

The elected Group II is drawn to a method for sterilizing heart valves by irradiation and one stabilizing protocol. The elected "species" [6/10/2003] are 1) stabilizing by temperature reduction and 2) irradiation gamma radiation.

Claims 2, 3, 6-14, 27, 28, 39-41, 49-53 and 81-88 remain rejected under 35 U.S.C. 102(b) and under 35 U.S.C. 103(a) as explained in the prior office action and reinstated herein below with respect to the claims as amended.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 2, 3, 27, 28, 39-41, 50-52 and 81-88 as amended remain rejected under 35 U.S.C. 102(b) as being anticipated by Campalani et al. [U].

Claims are directed to a method for sterilizing heart valves that are sensitive to radiation wherein the method comprises step of applying to heart valves a stabilizing process and step of irradiating heart valves with a radiation at effective rate for a time effective to sterilize heart valves wherein the stabilizing process is reducing the temperature of heart valves to a level effective to protect heart valves from radiation and wherein radiation is gamma radiation. Some

claims are/are further drawn to the stabilizing process and irradiation together being effective to protect from radiation. Some claims are further drawn to sterilizing the heart valves with biological contaminants and to the use of sensitizer in the method for sterilizing heart valves. Some claims are further drawn to temperature either less than ambient or below freezing point/glass transition point of the solvent surrounding the heart valves in the method for sterilizing heart valves. Some claims are further drawn to the recovery of the desired characteristics after sterilization greater than 50-100% of the pre-irradiated value in the method for sterilizing heart valves.

Campalani et al. teaches the aortic valve replacement with frozen gamma-irradiated homografts. In particular, the reference teaches a method for sterilizing heart valves or aortic valve homografts wherein the method comprises step of applying to heart valves a stabilizing process which is freezing to -70°C and step of irradiating the heart valves with gamma-irradiation with total dose 2.4 megarads or 24 kGy (page 559, col. 2, par. 2). The reference teaches storing of frozen 2 megarads gamma-irradiated heart valves for over a year before implantation and, thus, the radiation rate and time have been effective to sterilize the heart valves within the meaning of the claims 2 and 3. With respect to claims 50-52 and 81 the method for sterilization of the cited reference comprises irradiation at temperature below ambient which is below 0°C according to the applicants' definitions (specification page 27, last paragraph) and/or which is below freezing/glass transition point of a solvent which is either water in Hartmanns' solution or glycerol in the method of the cited reference. The reference teaches a recovery of some desired characteristics such as withstanding of the "tear out strength" test (page 559, col. 2, par. 2, last line) or survival of patients up to 16 years (fig. 2) and, thus, the recovery of desired

characteristics is considered to be 50 –100% for at least some of the gamma-irradiated heart valves within the meaning of the claims 82-88. The collected homografts were subjected to sterilization and, thus, they are reasonably considered to be non-sterile and/or containing at least some amount of biological contaminants within the meaning of the claim 28. According to the applicants' definitions sensitizer is a substance that targets microbe to be sensitive to irradiation (specification page 17, last paragraph). Thus, in the method for sterilization of the cited reference the components of the Hartmans'solution are considered to be sensitizers within the meaning of the claim 27, for example: spore forming microbial contaminants/pathogens would be rendered sensitive to irradiation upon spore germination in the presence of aqueous solution with nutrients, for example; water, salts, lactate in the Hartmann's solution.

Thus, the method of the cited reference comprises all active steps and structural elements of the claimed method. Therefore, the reference by Campalani et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 2, 3, 6-14, 27, 28, 39-41, 50-52 and 81-88 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over Campalani et al. [U] taken with Dziedzic-Goclawska et al. [IDS reference, Paper No. 12].

Claims 2, 3, 27, 28, 39-41, 50-52 and 81-88 as explained above. Claims 6-14 are further drawn to ranges of radiation rate being less than 0.3 kGy/hour, no more than 3.0 kGy/hour, more than 3.0 kGy/hour or at least 45kGy/hour in the method for sterilizing heart valves.

The reference by Campalani et al. is relied upon as explained above for the disclosure of the method for sterilizing of frozen heart valves by gamma-irradiation. The cited reference by Campalani et al. teaches 2.4 megarads as total dose but it is silent with regard to irradiation rate.

The reference by Dziedzic-Goclawska et al. teaches that the effectiveness of the sterilization of tissue allografts or homografts including heart valves (page 261, par. 1) is considered with regard to and/or depends on the resistance of different microorganism contaminating the tissues of homografts or allografts. The reference teaches acceptable total doses of radiation ranges, including 17 kGy or up to 40-50 kGy, depending on biological contamination and on the tissue related considerations (see pages 277-280). The cited reference also teaches various considerations related to the resistance of microorganisms to the sterilizing power of irradiation.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify radiation rate and/or time of exposure to radiation in order to achieve the required total dose of irradiation in the method disclosed by Campalani et al. with a reasonable expectation of success in sterilizing tissues homografts or allografts such as heart valves because the degree of radiation depends on a variable resistance of microbial contaminants/pathogens in the tissue allografts or homografts intended for reconstructive surgery {Dziedzic-Goclawska et al.}. One of skill in the art would have been motivated to adjust radiation rate and exposure time in order to achieve the required total radiation dose in order to prevent hazards of infectious disease transmission with tissues allografts including heart valves intended for reconstructive surgery as suggested by Dziedzic-Goclawska et al. The presently claimed method encompasses all possible radiation rate ranges from zero ("not more than 0.3",

claim 9) and up to unlimited upper level ("at least 45", claim 14). It is considered to be within the purview of ordinary skill in the art to adjust radiation rate ranges and time of exposure to achieve the acceptable total radiation dose required for proper sterilization of tissue allografts. The required standards and recommended protocols for tissue sterilization by irradiation are established in the art of the tissue sterilization as adequately demonstrated by Campalani et al. and Dziedzic-Goclawska et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary. The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicants' arguments filed 12/09/2003 have been fully considered but they are not persuasive.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by the reference by Campalani et al. applicants argue that the cited reference does not disclose the feature of the claimed invention that is reducing temperature of heart valve(s) to a level effective to protect from radiation during sterilization by gamma irradiation (responses pages 28-29). This is not true because the cited reference clearly teaches reduction of temperature to -70°C and irradiation of frozen heart valves by gamma-irradiation with the total dose 2.4 megarads or 24 kGy. The recovery of heart valve characteristics such as withstanding of the "tear out strength" test (page 559, col. 2, par. 2, last line) and survival of patients up to 16 years (fig. 2) as disclosed

by the cited reference demonstrate that the combination of temperature reduction and radiation were effective enough to protect and to sterilize heart valves within the meaning of the present claims in order to provide for the same benefit and success as intended by the instant invention.

With regard to the claim rejection under 35 U.S.C. 103(a) as being unpatentable over Campalani et al. taken with Dziedzic-Goclawska et al. applicants argue that the cited references do not disclose or suggest all of the features of the claims and/or that the reference by Dziedzic-Goclawska does not cure the "deficiencies" of the reference by Campalani (response page 30). However, applicants did not point out what particular features and/or deficiencies are being argued. With regard to the reference by Dziedzic-Goclawska applicants appear to argue that it does not disclose or suggest "reducing temperature" during sterilization of heart valves. However, this reference is relied upon for the teaching about radiation doses that are required for effective sterilization of the tissues intended for transplantation and about radiation resistance of microbial contaminants in the tissues intended for transplantation. Thus, the cited reference is in the same field and seeks to resolve the same problems as applicants.

Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Vera Afremova

AU 1651

February 18, 2004

V. Afremova

VERA AFREMOVA

PATENT EXAMINER